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Attributing mortality from temperature extremes: A time series analysis in Varanasi, India

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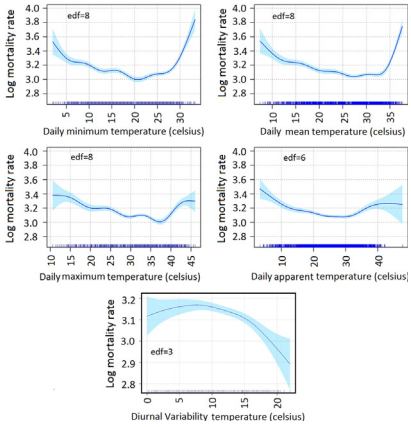
HIGHLIGHTS

- Mortality rate rises sharply during temperature extreme, both for cold & heat wave.
- During heat wave relative risk of mortality rises especially for female and infant.
- For different lag days excess mortality was noted during winter compared to summer.
- Compounded effect of temperature extreme considerably increased for air pollution
- Decrease in DTV has a negative impact on mortality, especially for males.

GRAPHICAL ABSTRACT

Exposure-response relationship of maximum, mean, minimum and apparent temperature and diurnal temperature variability.



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ABSTRACT

Climate extremes are often associated with increased human mortality and such association varies considerably with space and time. We therefore, aimed to systematically investigate the effects of temperature extremes, daily means and diurnal temperature variations (DTV) on mortality in the city of Varanasi, India during 2009–2016. Time series data on daily mortality, air quality (SO_2, NO_2, O_3 and PM_{10}) and weather variables were obtained from the routinely collected secondary sources. A semiparametric quasi-Poisson regression model estimated the effects of temperature extremes on daily all-cause mortality adjusting nonlinear confounding effects of time trend, relative humidity and air pollution; stratified by seasons. An effect modification by age, gender and place of death as semi-economic indicator were also explored. Daily mean temperature was strongly associated with excess mortality, both during summer (5.61% with 95% CI: 4.69–6.53% per unit increase in mean temperature) and winter (1.53% with 95% CI: 0.88–2.18% per unit decrease in mean temperature). Daily mortality was found to be increased by 12.02% (with 95% CI: 4.21–19.84%) due to heat wave. The DTV has exhibited downward trend over the years and showed a negative association with all-cause mortality. Significant association of mortality and different metric of temperature extreme along with decreasing trend in DTV clearly indicate the

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potential impact of climate change on human health in the city of Varanasi. The finding may well be useful to prioritize the government policies to curb the factors that causes the climate change and for developing early warning system.

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1. Introduction

Recent evidences of extreme weather events including heat, drought, and heavy precipitation have raised public and scientific interest in exploring potential adverse effects of climate-related events on human health. These climate-related events influence human health either by direct and/-or indirect exposure or through economic and social disruption (Smith et al., 2014). The adverse impacts of temperature extremes like heat waves and cold spells have been projected by many researchers, mainly over America (Kent et al., 2013; Sheridan et al., 2009), Asia (Lim et al., 2012; Wang et al., 2013; Mall et al., 2017), Australia (Bennett et al., 2014) and Africa (Egondi et al., 2015) with diverse increase in mortality rates (Gosling et al., 2009; Basu and Samet, 2002; Li et al., 2015). With the rise in global mean temperature, it has been projected with reasonable confidence that by the end of the 21st century heat waves will be more intense, more frequent and will last longer (Diffenbaugh and Scherer, 2011; Field, 2014). In contrast, low temperature events are expected to be exceedingly rare (Collins et al., 2013). In agreement with these projections, temperature extremes have considerably increased in several regions and vowed to be even more frequent in near future (Kirtman et al., 2013). Thus, understanding the effects of temperature extremes on human health is crucial for a country like India, owing both for its susceptibility to changing climate and for having low population resilience.

Several epidemiological investigations have linked heat wave with impacts on human health, including mortality (Kent et al., 2013; Guo et al., 2017) and morbidity (Carreras et al., 2015; Knowlton et al., 2008). Other studies claimed that heat waves have no added effects on human health (Gasparrini and Armstrong, 2011). Recent heat waves in Europe during 2003, 2007 and 2010 (Åström et al., 2013; Barriopedro et al., 2011), in Russia during 2003 and 2010 (Han et al., 2017; Luterbacher et al., 2004), in California during 2006 (Knowlton et al., 2008), and in India during 2010, 2013 and 2015 (Mazdiyasni et al., 2017) led to numerous epidemiological studies with diverse conclusions. In contrast, cold spells related mortality is mostly under reported (Chen et al., 2017; Guo et al., 2014). Increased mortality during heat or cold events has been mainly attributed to cardiovascular diseases (CVD), cerebrovascular and chronic respiratory diseases (RD, Kilbourne, 1999; Gosling et al., 2017; Hajat et al., 2014). Heat waves are reported to increase blood viscosity (due to dehydration), cardiac output and blood cholesterol, resulting in blood clot, hypotension and endothelial cell damage, especially for people with pre-existing atrial fibrillation (Cheng and Su, 2010). In contrast, cold stress influences vasoconstriction and high blood pressure, sympathetic nervous activities, platelet aggregation and red blood cell count (Cheng and Su, 2010). Symptoms may further aggravate in combination with air pollution and humidity (Yang et al., 2019), while population demographics, susceptibility, physiologic acclimatization and socio-economic resilience also influence the severity of the effects (Kinney et al., 2008).

Possible association of heat stress with human mortality has been explored by many researchers, suggesting considerable spatial/-community level variations (Anderson and Bell, 2009; Guo et al., 2012) and temporal/-seasonal implications (Bennett et al., 2014; Carson et al., 2006). Comparison of such impacts among different studies is however complicate, as they usually differ in terms of climatic zones (tropical/temperate), methodology (time-series/case-crossover design), and population resilience. Besides, scientific evidence on the effect of extreme temperature on the public health in countries with developing economy are extremely rare. This has emphasized the need to initiate a comprehensive research on the possible influence of extreme temperatures on premature mortality in Varanasi, located at the heart of Indo-Gangetic Plain (IGP), South Asia. The region is reported to have influenced by very high pollution load, both in terms of airborne fine particulates (Kumar et al., 2017, 2018; Singh et al., 2017; Mhawish et al., 2017, 2019; Dey and Di Girolamo, 2011) and short-lived climate pollutants (Shukla et al., 2017; Singh et al., 2018). Therefore, daily all-cause mortality, air quality and meteorological variables were explored for 2008–2017, to assess if extreme temperature and the diurnal temperature variation (DTV) have any influence on mortality. Possible implications of such analysis may be in developing early warning systems, robust adaptation policies and for improving mitigation strategies.

2. Data and methods

2.1. Study area

Varanasi city (25°16′N, 82°59′E; 82 m MSL) is located in the center of the Indo-Gangetic plain of Northern India (Fig. 1). The city typically witnesses humid subtropical climate with four distinct seasons: cold and moist winter (DJ), warm and dry summer (pre-monsoon, MAMJ), monsoon (JAS), and post-monsoon (ON). The maximum temperature reaches up to 46 °C in the summer months while minimum temperature usually drops as low as 2 °C during winter (Murari et al., 2017). The city occasionally witnesses a distinct hot and dry heat wave (locally referred as *Loo*) during summer, and cold spells during winter. Varanasi's urban agglomeration supports a huge population (12 million in year 2011; MHA, 2011), with a very high population density (14,598 Km^{-2}) and frequent influx of pilgrims and tourists (Table S1).

2.2. Data availability

Daily mortality data for 2009–2016 (all inclusive) was collected from the office of Municipal Corporation of Varanasi. The dataset includes: 1. date of death, 2. cause of death classified according to the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10), and 3. the residence location, 4. place of death. Mortality data was classified into all-cause mortality (ICD-10 codes A00–R99), cardiovascular diseases (ICD-10 codes I00–I99) and respiratory diseases (ICD-10 codes J00–J98), according to the gender (male/female), age (≤4, 5–44, 45–64, ≥65 years) and place of death (institutional and non-institutional deaths). Daily meteorological data (daily minimum, maximum and mean temperature; relative humidity, RH) was obtained from the India Meteorological Department, New Delhi. Ambient air quality in terms of PM_{10}, SO_2, NO_2 and ground-level O_3 concentration from 2009 to 2016 was assessed from Real-time Air Quality Data inventory of the Central Pollution Control Board (https://app.cpcbccr.com/ccr). The air quality monitoring station is in the city center and is mainly influenced by emissions from residential and commercial activities (Singh et al., 2018). Hourly concentration of individual pollutants was initially checked for data quality and outliers, and further averaged to 24 h.

2.3. Statistical methods

Daily mortality, temperature, relative humidity and ambient concentration of air pollutants were summarized by descriptive statistics. The distribution of mortality and temperature were visualized by panels

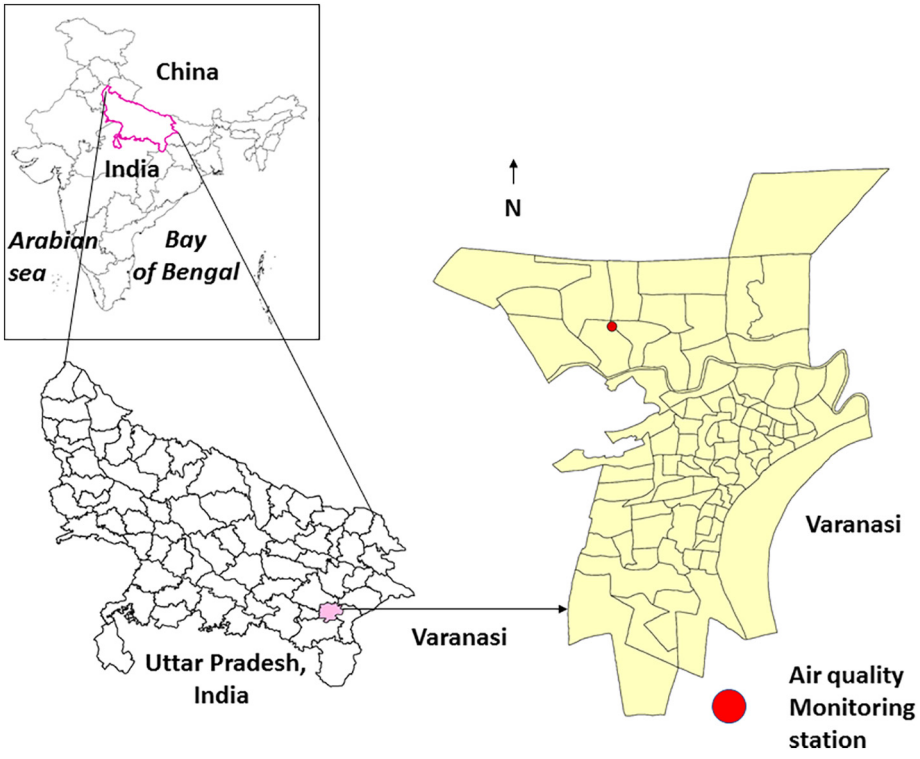

Fig. 1. Map of Varanasi including air quality monitoring station.

of time series plot. Temperature extremes are mainly defined in arbitrary, while most commonly referred as high/-low temperature above a certain threshold (either physiological or community based) for few successive days (Robinson, 2001; Guo et al., 2017; Song et al., 2017). Heat wave was defined as an event during summer with daily mean temperature remain equal or above the 95th percentile of annual mean (≥34.5 °C) for at least 3 consecutive days. Cold spell was defined as an event during winter with daily mean temperatures equal to or below the 5th percentile of annual mean (≤14.7 °C) for at least 3 consecutive days [moving average lag (0–2)]. The distribution of temperature ranges and number of cold wave and heat wave days were reported by histogram and line diagram, respectively. Diurnal temperature variability (DTV) was derived as the difference between daily maximum and minimum temperature. To compare the long-term trend of temperature and DTV, they were smoothed over time by penalized cubic spline and visualized by smoothed curves.

The effects of daily mean temperature on mortality was estimated by each of the three seasons; summer (AMJ), winter (DJF) and other season (inclusive of rest months), adjusting for other nonlinear confounders such as time trend, relative humidity, ambient air pollution and days of the week. The following semiparametric quasi-Poisson regression model with season specific regression coefficients of temperature was used:

$$Log\{E[(mortality)_t]\} = \alpha + \beta_w\left(temp_t \times I_t^{(w)}\right) + \beta_s\left(temp_t \times I_t^{(s)}\right) + \beta_o\left(temp_t \times I_t^{(o)}\right) + \sum_{j=1}^{p} f_j(x_{jt}) + \sum_{k=2}^{7} \alpha_k I_t^{(k)} \quad (1)$$

where, β_w, β_s & β_o are the regression coefficients corresponding to temperature during winter, summer and other season respectively, $I_t^{(w)} = \begin{cases} 1, & if\ t^{th}\ day\ falls\ in\ winter \\ 0, & otherwise \end{cases}$, similarly $I_t^{(s)}$ & $I_t^{(o.)}$ for summer and other seasons; $f_j(x_{jt})$ is the jth smoothed function (penalized cubic smoothing spline) of x_{jt}'s-nonlinear confounders (j = 1,2,…,p) where p stands for number of nonlinear confounders such as time, relative humidity, PM_{10}, SO_2, NO_2 and O_3 ($p = 6$); α_k is the intercept for k^{th} day of week (starting from Monday to Saturday, Sunday is in reference category), $I_t^{(k)} = \begin{cases} 1, & if\ k^{th}\ dow \\ 0, & otherwise \end{cases}$.

It is important to mention that the association of daily mean temperature during summer is expected to be directly proportional to mortality, hence positive regression coefficients should be interpreted as risk and negative as protective. But for winter the association is expected to be inverse and hence negative regression coefficient should be considered as risk while positive as protective.

The effects of extreme temperature such as heat wave and cold wave on daily mortality were estimated using quasi-Poisson semi-parametric regression model:

$$Log\{E[(mortality)_t]\} = \alpha + \beta_{hw} I_t^{(hw)} + \beta_{cw} I_t^{(cw)} + \sum_{j=1}^{p} f_j(x_{jt}) + \sum_{k=2}^{7} \alpha_k I_t^{(k)} \quad (2)$$

where, β_{hw} & β_{cw} are the regression coefficients corresponding to heat wave and cold wave, $I_t^{(hw)} = \begin{cases} 1, & if\ heat\ wave\ on\ t^{th}\ day \\ 0, & otherwise \end{cases}$, similarly, $I_t^{(cw)}$ for cold wave; rest are as before time, daily mean temperature, relative humidity, PM_{10}, SO_2, NO_2,O_3 and date of the week. The effect of DTV on mortality was estimated from the Eq. (2) replacing 2nd and 3rd terms by $\beta_{dv}(DV)_i$.

Further, in order to investigate the effect modification in temperature-mortality association by individual characteristics, we fitted above models separately for each individual factor such as age, gender, and place of death. The age/-gender/-place of death specific regression coefficients were also compared within the group by Wald χ^2-test to measure the equality of regression coefficients assuming covariance to be zero (Diggle et al., 1994).

Additionally, the dose-response curve of mortality and different temperature metrics adjusting other confounding factors were generated to observe the changes in mortality caused by the different level of temperature exposure. The dose response curves were generated by applying penalized cubic spline function of the temperature metrics in the Eq. (1) ignoring stratification by season which estimated degrees of freedom based on Generalized Cross Validation (GCV) score. The estimated degrees of freedoms (edf) were embedded into Fig. 8.

Population vulnerability to climate extremes are measured both in terms of sensitivity and adaptive capability. To analyze individual's adaptive capability was beyond our scope therefore, we emphasized on sensitivity analysis. We performed different sensitivity analyses. First, we stressed on exploring specific temperature metrics which defines mortality better, as may be the case that certain temperature metrics may impact strongly on individual. We have carried out the sensitivity analysis to evaluate how does estimates vary over selection of different temperature metrics (maximum and minimum temperature, mean temperature, apparent temperature and diurnal temperature) within the core model. We then considered the possibility that mortality not only depends on the current day exposure, but also on previous days' exposure (time lag effects). We therefore, applied a restricted distributed lag model up to 7 days' lag with polynomial of degree two with Eq. (1) (Schwartz, 2000) and single lag model up to 7 days lag. Further, the nonlinear association of temperature metric and sensitivity of the choice of degrees of freedom (1 to 3 degrees of freedom) of temporal effect on mortality at season specific analysis was also explored.

The data was analysis by statistical software R version 3.5.1 (R Core Team, 2018); the R -package "mgcv" (version 1.8–18.) (Wood, 2006) and "dlnm" (version 2.3.2.) (Gasparrini, 2011) were used in subsequent analysis.

3. Results and discussion

Descriptive statistics of daily all-cause mortality, RD and CVD associated mortality, meteorology and air quality are summarized in Table 1. Mean (±SD) daily all-causes mortality for 2009–2016 was 22 (±6), among which 60% were male. Daily mean (±SD) male mortality was higher (13 ± 4) compared to daily mean (±SD) female mortality (9 ± 4). Again, within all-cause mortality, the cases due to RD and CVD accounted 29%, 65% of which were male referring their added vulnerability to the exposure to outdoor environment. The average lifespan in Varanasi was computed as 59 years, well below in reference to national (68.6 years) and global averages (72.0 years, WB, 2018). There was also a specific seasonal pattern in the daily all-cause mortality, with slightly excess mortality mainly during winter (28%) compared to summer (24%) and monsoon (23%). Table 1 also summarizes the ambient air quality in Varanasi experienced from 2009 to 2016 (all inclusive). Mean (±SD) PM_{10} concentration was 219 (±136) μg/m^3, with the yearly annual mean varying from 188 to 320 μg/m^3, well exceeding World Health Organization standard (50 μg/m^3) and the Indian national ambient air quality standard (100 μg/m^3). Air quality in terms of PM_{10} was particularly severe having 87% of the monitoring days (n = 1905) exhibit non-attainment of the national standard. PM_{10} concentration was highest during winter (320 ± 118 μg/m^3) and post-monsoon (267 ± 109 μg/m^3) while lowest during rainy monsoon season (115 ± 96 μg/m^3; Kumar et al., 2017; Singh et al., 2018). In contrast, the abundance of trace gases was comparatively low and remained mainly within the standard. Concentration of NO_2 and SO_2 was lowest during monsoon (NO_2: 13 ± 6; SO_2: 3 ± 2 μg/m^3) before rising to its peak during winter (NO_2: 30 ± 11; SO_2: 4 ± 2 μg/m^3), while concentration of O_3 was highest in pre-monsoon (33 ± 19 μg/m^3; Shukla et al., 2017). Among the seasons, winter was the most polluted season in every aspect followed by post-monsoon while monsoon was relatively clean (Fig. S1).

All-cause mortality time series, four different temperature metrics, and a time series of the heat and cold event are presented in Fig. 2. Over the period, the city has experienced on an average 8 episodes of heat waves in each year (91 total), primarily in May and June, and 8 episodes of cold waves in each year from December to February (97 total). The daily mean mortality during temperature extreme days (28) increased by 27% compared to the normal days (22). A clear declining

Table 1
Summary of the mortality, meteorological conditions and air pollution in Varanasi from 2009 to 2016.

Variable	No. of observation	Mean	SD	Median	Maximum	25th percentile	75th Percentile
Daily death counts							
All cause mortality	64,712	22.15	6.1	22	78	18	25
Respiratory disorder (RD)	222	0.3	0	0	0.08	0	0
Cardiovascular disorder (CVD)	1996	1.42	0.7	1	5	1	2
Mortality classified by gender							
Male	38,640	13.22	4.3	13	51	10	16
Female	26,072	8.92	3.5	9	34	6	11
Mortality classified by age							
Age (0–4)	4132	1.37	1.3	1	8	0	2
Age (5–44)	10,130	3.47	2.0	3	13	2	5
Age (45–64)	17,709	6.06	2.6	6	20	4	8
Age (65 and above)	32,741	11.21	4.2	11	46	8	13
Mortality classified by place of death							
Institutional death	44,585	6.9	2.9	7	22	5	9
Non-institutional death	20,127	15.3	4.9	15	61	12	18
Meteorological parameters							
T.max (°C)	2922	31.56	6.6	32.4	46.2	27.0	35.8
T.min (°C)	2922	20.05	7.0	21.8	39.6	13.8	26.2
T.mean (°C)	2922	25.81	6.4	27.7	40.6	20.1	30.7
RH (%)	2922	63.75	20.1	63.0	98.0	44.0	75.0
AT (°C)	2365	28.56	7.4	26.4	47.7	20.5	31.0
Air pollution parameters							
PM_{10} (μg/m^3)	2181	219.21	135.7	208.2	901.6	97.3	317.6
SO_2 (μg/m^3)	2344	3.93	4.9	3.1	102.6	2.2	4.4
NO_2 (μg/m^3)	2278	20.64	11.8	19.4	132.0	12.2	28.4
O_3 (μg/m^3)	2368	23.03	16.0	18.2	151.1	11.3	31.1

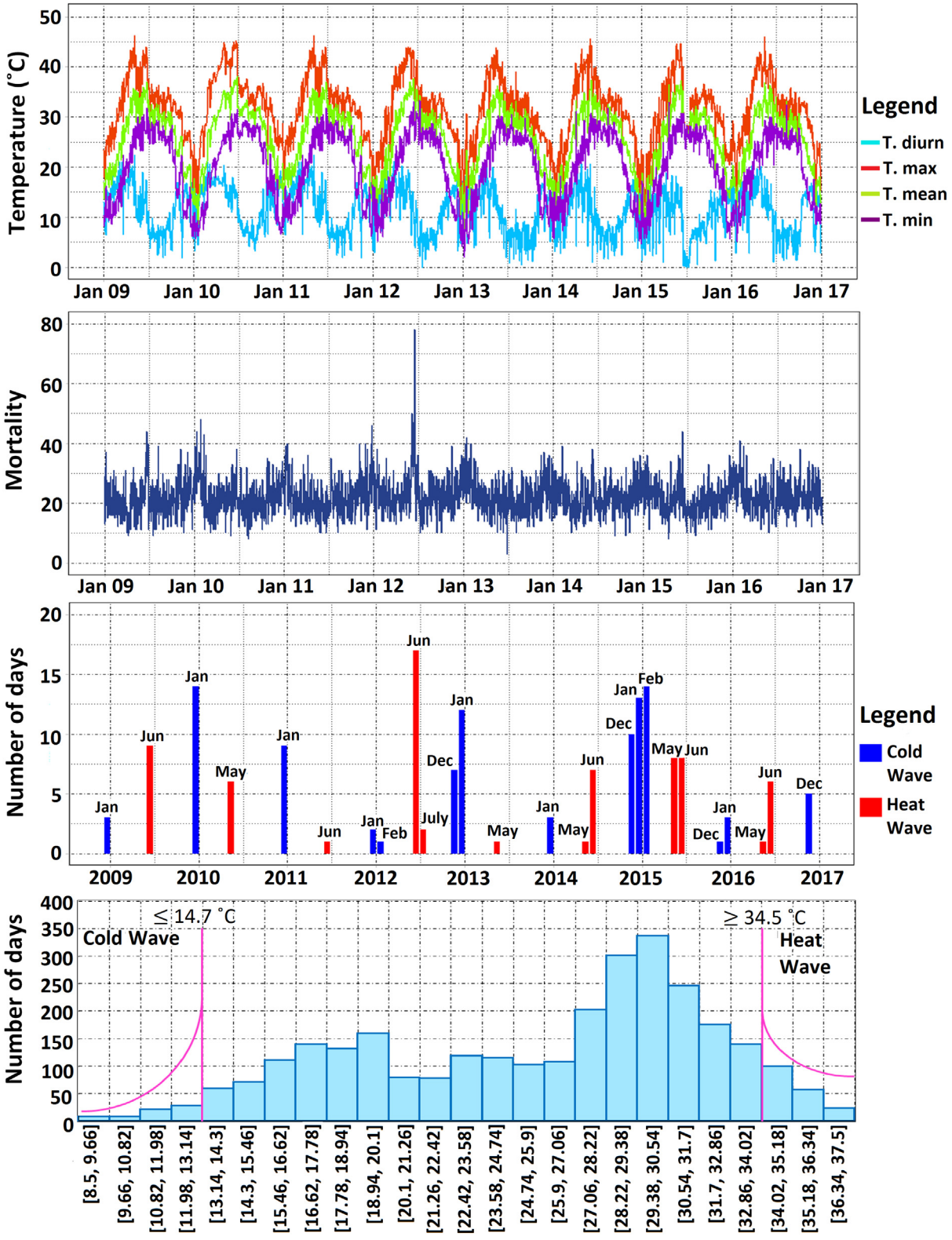

Fig. 2. Distribution of daily (a) maximum, minimum, mean and diurnal temperature, (b) all-cause-mortality, (c) monthly distribution of heat wave and cold spell, (d) Temperature distribution of 3-day moving average of mean temperature showing different temperature range for heat wave (≥95 percentile) and cold spell (≤5 percentile).

trend of maximum and mean temperature in all the centiles were also noted, with an increasing trend of minimum temperature (Fig. S2). Such an increase in the daily minimum temperature may be crucial as heat stress related mortality are reported to be higher when nights are especially warmer (Murage et al., 2017). The variation in the daily mean temperature from 2009 to 2016 indicates an overall decrease (0.7 °C, Fig. 3), opposite to the reported increasing trend over India (0.5 °C; Mazdiyasni et al., 2017). The DTV also reduced sharply until

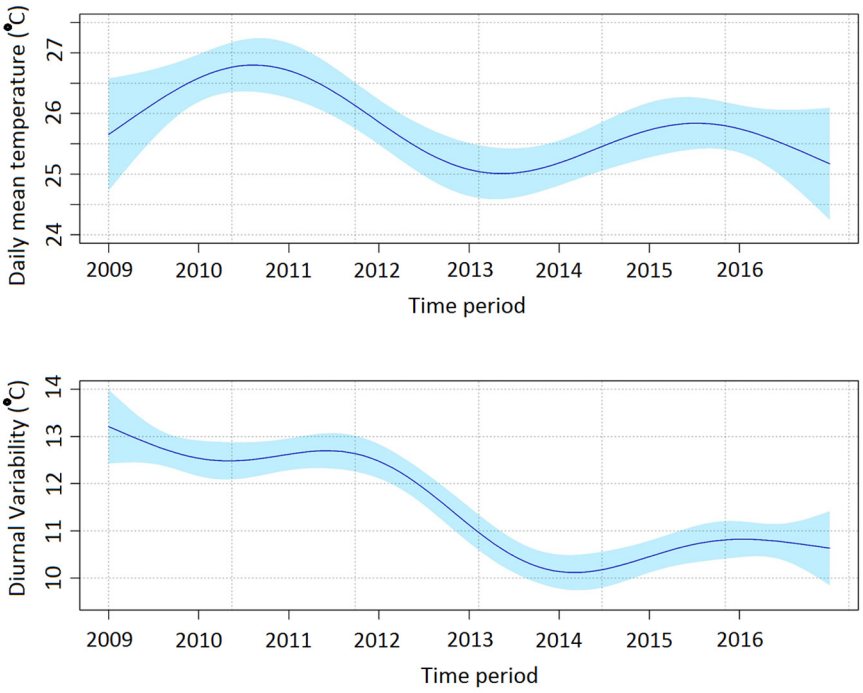

Fig. 3. Distribution of daily mean temperature and diurnal variability over time.

2015 (2.2 °C), with an overall reduction of 0.8 °C between 2009 and 2016. The decrease in DTV was primarily influenced by the decrease in daytime temperature (−0.012 °C; 0th centile) and the increase in minimum temperature at higher centiles (0.004 °C; 100th centile). The DTV centile plot shows a clear declining trend, mostly in the lower centiles (−0.013 °C; 5th centile; Fig. S2), which is a clear indication of reduction in the daily difference between maximum and minimum temperature. Overall, decline in the diurnal variability of the temperature was consistent with the global observations, and has often been associated with increased mortality and human health problems (Guo et al., 2014, 2016; Carreras et al., 2015; Yang et al., 2018).

All statistical analysis was made using mean temperature as it was most strongly associated with excess mortality (Table 2). The details have been discussed in the sensitivity analysis part. We also stratified the mortality by age, sex, cause of death and place of death as these are known to influence the association between temperature and human health (Carreras et al., 2015). Considering the consistent decline in DTV over Varanasi, we also examined its effects on mortality.

3.1. Mean temperature and daily mortality

The association between daily mean temperature and mortality varied considerably between the seasons and among various age groups (Fig. 4). During summer, daily 5.6% all-cause mortality was noted compared to the daily 1.5% all-cause mortality during winter. Mortality rates for male were slightly higher in winter (−1.71%, 95% CI: −2.51, −0.90%) whereas for female they were higher during summer (6.03%, 95% CI: 4.63, 7.43%). We also found evidence that increase in all-cause mortality was highest for people ≥65 years of age (−2.71% in winter to 6.83% in summer) and gradually reduced with the decrease in age, except for 0–4 years. The shift in daily all-cause mortality with age was identical for both summer and winter months, while the extent of change in mortality was comparatively higher during summer. Similar evidences of strong association between daily mean temperature and mortality were reported in United States and China for summer months (Davis et al., 2016; Zhang et al., 2017). In India, Mazdiyasni et al. (2017) also reported a 146% increase in daily heat-related mortality based on a single event of 0.5 °C increase in the summer mean temperature. We also found higher mortality for non-institutional deaths (those dying outside the hospital) compared to institutional deaths (those dying within the hospital). In absence of direct observation, place of death was considered as a proxy to socio-economic condition (Zhang et al., 2017; Ma et al., 2015). Death outside hospital (Non-Institutional

Table 2
Effects of different metrics of daily temperature on mortality for different seasons.

Temperature metric	Season	% Change in mortality/unit change in temperature	RR(95% CI)/unit change in temperature
Min	Winter	−1.14(−1.78,−0.5)	0.989 (0.982,0.995)
	Summer	4.81(4.03,5.59)	1.049 (1.041,1.057)
	Other Seasons	0.18(−0.23,0.59)	1.002 (0.998,1.006)
Mean	Winter	−1.53(−2.18,−0.88)	0.985 (0.978,0.991)
	Summer	5.61(4.69,6.53)	1.058 (1.048,1.067)
	Other Seasons	0.03(−0.49,0.56)	1(0.995,1.006)
Max	Winter	−1.03(−1.55,−0.51)	0.99(0.985,0.995)
	Summer	2.95(2.18,3.71)	1.03(1.022,1.038)
	Other Seasons	−0.05(−0.66,0.55)	0.999 (0.993,1.006)
AT	Winter	−1.19(−1.65,−0.73)	0.988 (0.984,0.993)
	Summer	1.48(0.97,1.99)	1.015(1.01,1.02)
	Other Seasons	0.14(−0.23,0.51)	1.001 (0.998,1.005)
DTV	Winter	−0.75(−1.37,−0.13)	0.992 (0.986,0.999)
	Summer	−1.32(−2.03,−0.61)	0.987(0.98,0.994)
	Other Seasons	−0.38(−0.95,0.2)	0.996 (0.991,1.002)

Note. The abbreviations used in the table are: Min = Minimum Temperature; Mean = Mean Temperature; Max = Maximum Temperature; AT = Apparent Temperature; DTV = Diurnal Temperature Variability.

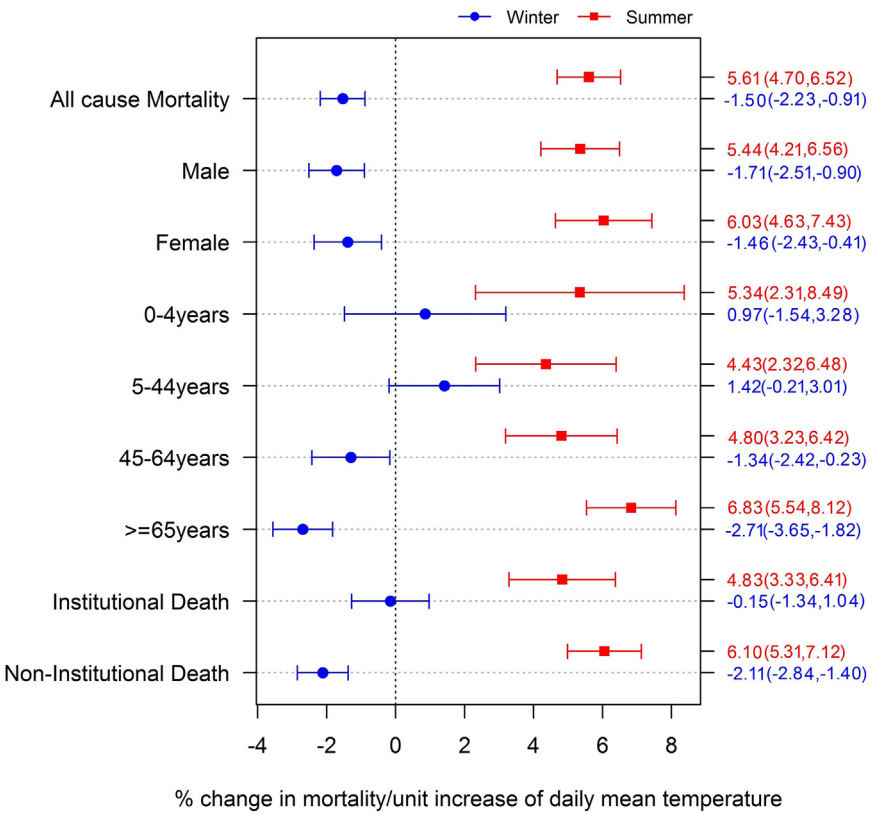

Fig. 4. Percent change in mortality associated with increase in mean temperature.

death) possibly reflect inaccessibility to health insurance, health care facilities and poor housing condition which make population even more vulnerable, thereby increases the exposure intensity to unusual temperature. Percent increase in mortality due to non-institutional deaths were higher in summer (6.10%, 95% CI: 5.31, 7.12%) compared to winter (2.11%, 95% CI: 2.84, 1.40%).

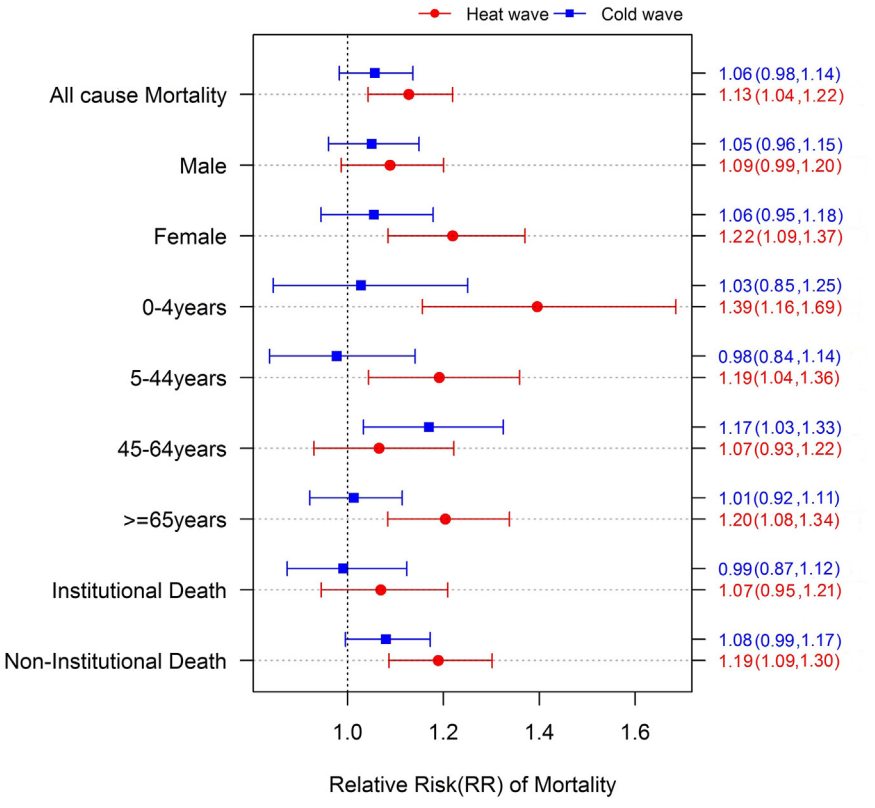

Fig. 5. Relative risk of cold spells and heat waves on daily number of mortalities.

3.2. Temperature extremes and daily mortality

We have assessed the mortality risk in terms of pre-defined cold waves and heat waves. Fig. 5 shows mortality in Varanasi from 2009 to 2016 stratified by place of death, sex and age. Model results suggest that temperature extremes amplify the relative risk (RR) of all-cause mortality in Varanasi for both heat waves (RR 1.13, 95% CI: 1.04–1.22) and cold spells (RR 1.06, 95% CI: 0.98–1.14). For cold spells, there was no significant difference in the RR between males and females. However, for heat waves the RR for males (RR 1.09, 95% CI: 0.99–1.20) was much smaller than for females (RR 1.22, 95% CI: 1.09–1.37). Interestingly, the highest RR of cold spells was especially noted for the 45–64 years age group (RR 1.17, 95% CI: 1.03–1.33) whereas, for heat stress the most sensitive age group was <4 years (RR 1.39, 95% CI: 1.16–1.69). There was evidence that relative risks of mortality to heat wave was more closely associated to population age as both elderlies (≥65 years) and children (≤4 years) suffers the maximum deaths compared to others. The mortality risk was also higher in non-institutional deaths and the effect was more prominent during heat wave.

Several studies from Europe, Latin America and China reported increased risks from temperature stress for the elderly and socioeconomically deprived individuals (Chen et al., 2017; Han et al., 2017; Guo et al., 2017; Åström et al., 2013; Sheridan et al., 2009; Wolf et al., 2014). Chen et al. (2017) reported a high mortality risk in Texas, USA, ranging between 0.1 and 5% for 1 °C decrease in temperature below the cold threshold. Han et al. (2017) reported a similar association for cold (RR 1.08, 95% CI: 1.06–1.11) and heat (RR 1.02, 95% CI: 1.00–1.05) waves in Jinan, China. A significant increase in heat stress related mortality in Stockholm, Sweden was also reported what would have occurred without climate change (Åström et al., 2013). Effect of extreme temperature is also constrained by community level characteristics. Guo et al. (2017) emphasized that heat wave related mortality is more related to the community itself, based on its sensitivity and adaptability, resulting in excess mortality more frequently over the cold regions. Ma et al. (2015) considering 66 communities across China, reported 5% excess deaths associated with heat waves that was potentially modified by age, gender, place of death and education attainment.

We also observed that the associations between mortality and extreme temperature are substantially confounded by air pollution. The estimated effect of extreme temperature on total mortality was increased during heat wave (3.2%; Age: 0–4 years) and cold wave (5.5%; Age: 45–64 years) when the model was controlled for airborne pollutants (particularly PM_{10}, Table S2). The results are supported by similar observation from Europe (Fischer et al., 2004; Stedman, 2004), France (Filleul et al., 2006; Dear et al., 2005; Benmarhnia et al., 2014), Australia (Buckley et al., 2014) and China (Yang et al., 2019). Yet, these studies present heterogeneous finding as aerosol composition varies between geographical regions, and individual characteristics such as age, gender, socio-economic condition, alcohol consumption and smoking also alter the relationship (Bravo et al., 2016).

3.3. Diurnal temperature variation and daily mortality

Diurnal temperature variability (DTV), defined as the difference between maximum and minimum temperature, decreased sharply in Varanasi until 2015, mainly due to the decrease in daytime temperature (−0.012; 0th centile; Fig. S2). The importance of declining trend in lower centiles of DTV can be perceived in a manner that it attributes to a much less difference between maximum and minimum temperature. Fig. 6 denotes the change in mortality (%) with respect to unit change in diurnal temperature. Overall, mortality associated with DTV was −0.61% (95% CI: −1.01, −0.25%), marginally higher for institutional death (−0.9%, 95% CI: −1.51, −0.22%), and having more detrimental effect on males (−0.88%, 95% CI: −1.30, −0.36%) compared to females (0.23%, 95%CI: −0.82, 0.48%). The association with all-cause mortality was high (−1.32%, 95% CI: −2.24, −0.44%) until 2015 due to the change in DTV (till 2015), before being reduced to −0.63% (95%

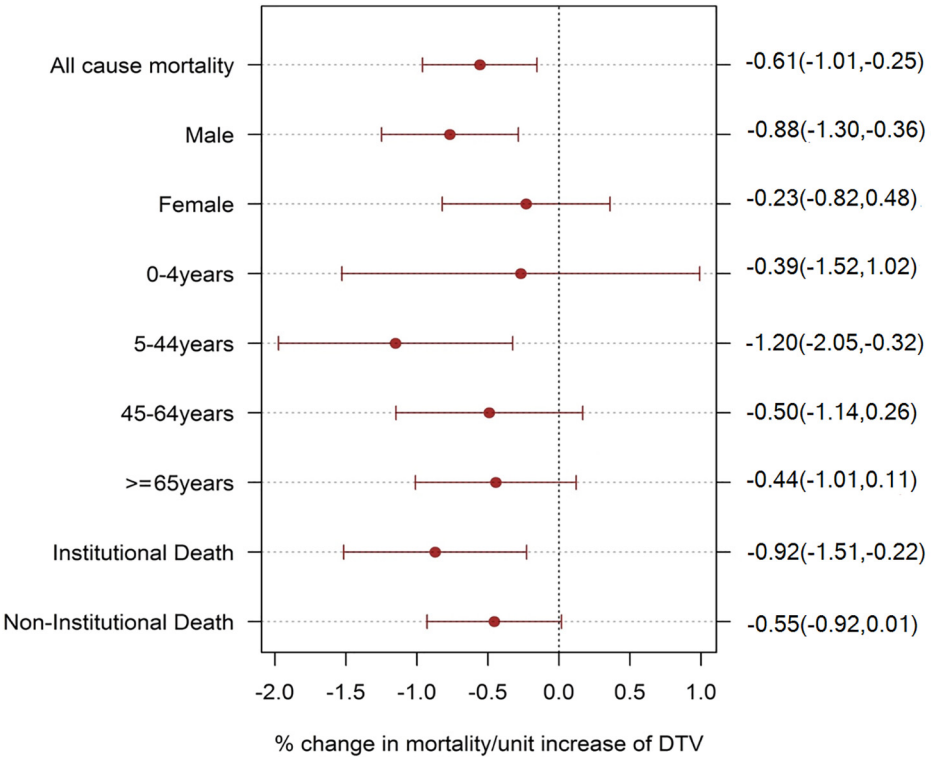

Fig. 6. Percent change in mortality associated with increase in diurnal variability.

CI: −1.12, −0.24%) for 2009 to 2016. The largest effect of DTV on mortality (1.20%, 95% CI: −2.05, −0.32%) was noted for people aged 5–44 years while both elderly and infants were found less susceptible to DTV.

Several multicountry and multicommunity studies reported incremental risk of mortality associated with the change in DTV (Carreras et al., 2015; Guo et al., 2016; Lee et al., 2018; Yang et al., 2018). The health implications are mostly reported in terms of obstructive pulmonary diseases (Song et al., 2008), coronary heart diseases (Cao et al., 2009) or cerebrovascular diseases (Smolensky et al., 2015). Lee et al. (2018), Murage et al. (2017), Basu and Samet (2002) suggested that the decreasing temperature variability reduces the possibility of heat relief, particularly at night. Its impact become more stern when the daytime temperatures also remain very high (Murage et al., 2017; Kovats and Hajat, 2008). However, in most of the cases health implication were not isolated in terms of sex or level of education, but by means of age, except by Yang et al. (2013), Murage et al. (2017) and Yang et al. (2018). In Guangzhou, China, a 1 °C increase in DTV at lag of 0–4 days was reported to cause 0.47% (95% CI: 0.01%–0.93%) increase in non-accidental mortality (Yang et al., 2013) whereas in London elevated nighttime temperature contribute to high mortality risk (RR 1.7%, 95% CI: 1.3–2.1), mainly for patients with chronic ischemic disease and stroke, and for people <65 years (Murage et al., 2017). In a multicity study in China by Yang et al. (2018), an increase in stroke mortality was reported at 0–10 lag days for each 1 °C increase in DTV for hot (0.12%, 95% CI: −0.26, 0.51%) and cold days (0.67%, 95% CI: 0.26–1.07%). However, spatial heterogeneity does exist among the cities, and human factors like alcohol consumption, arbitrary life style and night shifts also influences the chance of mortality during low DTV.

3.4. Sensitivity analysis

We have analysed all-cause mortality against different temperature metrics, adjusting for the time trend, air pollution, relative humidity and DOW (Table 2). The daily mean temperature was most strongly associated with excess mortality, both during summer (5.61%; 95% CI: 4.70–6.52%) and winter (1.50%; 95% CI: −2.23, −0.91%). Sensitivity analysis bring forth that the effect estimates varied by exposure days and remained significant at lag 0–7 days for both summer and winter. For example, with increase in cumulative lag exposure, effect estimates for mortality has been increased during winter while it has decreased during summer (Fig. 7). The detailed description has been provided in Table S3 in reference to the mean temperature exposure. The magnitude of mortality risk was highest at lag 0–6 (current day of death) for summer mean and minimum temperature (cumulative lag days) and summer maximum temperature. The cumulative lag effect of winter maximum temperature on mortality peaked at lag 0–2 (RR 0.98; 95% CI: 0.97, 0.99). Effect estimates for minimum temperature during winter peaked at lag 0–2 (RR 0.97; 95%CI: 0.96, 0.98) and at lag 0–2 days for winter mean temperature. The lag choices could adequately capture the adverse effects of high/low temperature on mortality. Similar lag choices of 0–7 days for heat effects on cardiovascular and cerebrovascular diseases were reported by Murage et al. (2017), while a moving lag average 1–5 days were used by Guo et al. (2016) for cold stress. Apart from cumulative lag model the single lag model were also explored. With increase in lag days, the single-day lag shows protective effect during summer while increase in associated risk during winter. We observed the maximum risk at lag 0 for summer (RR 0.997; 95% CI: 0.994, 1.000) while during winter maximum risk was noted for lag 7 (RR 1.000; 95% CI: 0.995, 1.005).

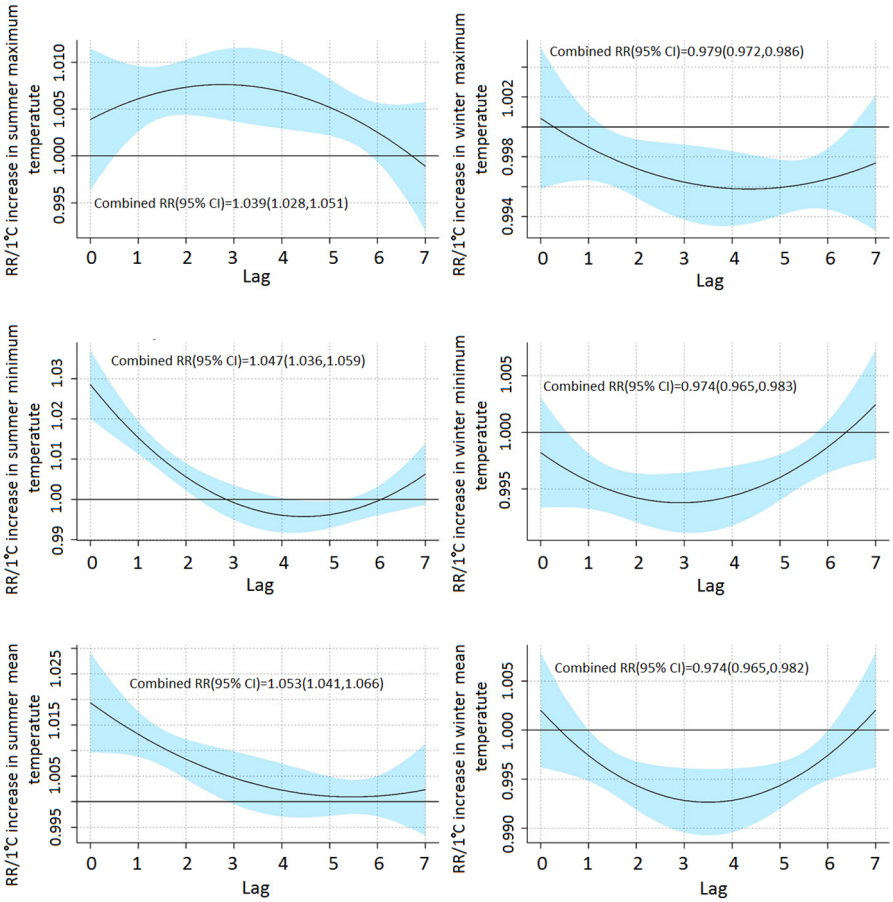
RR/1°C increase in summer maximum temperatute
Combined RR(95% CI)=1.039(1.028,1.051)
RR/1°C increase in winter maximum temperatute
Combined RR(95% CI)=0.979(0.972,0.986)
RR/1°C increase in summer minimum temperatute
Combined RR(95% CI)=1.047(1.036,1.059)
RR/1°C increase in winter minimum temperatute
Combined RR(95% CI)=0.974(0.965,0.983)
RR/1°C increase in summer mean temperatute
Combined RR(95% CI)=1.053(1.041,1.066)
RR/1°C increase in winter mean temperatute
Combined RR(95% CI)=0.974(0.965,0.982)
Lag

Fig. 7. Lag patterns for maximum, minimum and mean temperature effect on non-accidental mortality.

In general, heat related mortality was associated with a shorter lag (0–3 days), while cold related mortality last longer (0–21 days, Anderson and Bell, 2009; Conlon et al., 2011). For this study, change of lag (0–7) did not significantly influence the effect estimates during summer, while slightly higher estimates were noted during winter using maximum and minimum temperature and slight lower estimates were recorded for mean temperature. The nonlinear association of temperature metric on mortality at season specific analysis was also explored but found to be perfectly linear. We also explored the sensitivity of the choice of degrees of freedom (1 to 3) of temporal effect on mortality in season specific analysis as noted in Table S3. We didn't find any noticeable changes in the effects of temperature metric on mortality, hence was not reported.

3.5. Exposure-response curve

Fig. 8 indicates the exposure-response curves for different temperature indices associated mortality with 95% confidence interval. In general, a non-linear association between temperature and mortality was noted with an overall increase in mortality for increasing temperature. The exposure response curves for the maximum and the apparent temperature were identical, with small mortality risks till 35 °C. However, the mortality risks increased by 21% for daily maximum temperature >37 °C. An identical exposure-response curve was also evident for the daily minimum temperature and the daily mean temperature. Namely, mortality risk increased for daily minimum temperature >27 °C and for daily mean temperature >33 °C. This clearly establish the detrimental health impact of increase in daily minimum temperature in continuation with increase in daily means, which possibly induce additional stress to patients with chronic ischemic and stroke, and in younger population (Murage et al., 2017). The early morning hour deaths from stroke, heart failure and ischemic diseases (Elliott, 1998) is most probably due to disturbed circadian rhythm, known to regulate physiological mechanism (Moser et al., 1994). Similar results were also noted for DTV <7.0 °C, with subsequent decrease in mortality for DTV >15 °C. Due to limited data in two extremes of the curve, confidence bands <7 °C and >15 °C were found to be quite wide. However, DTV exhibited almost linear association between 7 °C and 15 °C with daily mortality count which was quite robust due to narrow confidence band. A non-linear association between DTV and mortality was reported also by Zhang et al. (2018). However, in contrast to the reports of increase in mortality with extremely high DTV (Zhang et al., 2018; Ding et al., 2015), we found elevated level of mortality with decrease in DTV for Varanasi. Such observation was identical to the published reports over China (Luo et al., 2013).

Several caveats to this analysis do exist. First, as the study focused on a single city, the results may vary in other environmental conditions. Second, the meteorological and air pollution variables were retrieved from a single available monitoring station, which may lead to some sort of variations in individual exposure. However, assuming that the variables would not vary significantly over a small urban geographic area, the single station would be able to display the uniformity (Zhang et al., 2017). Due to data constraint, we did not account for the individual level characteristics e.g. socioeconomic conditions, literacy,

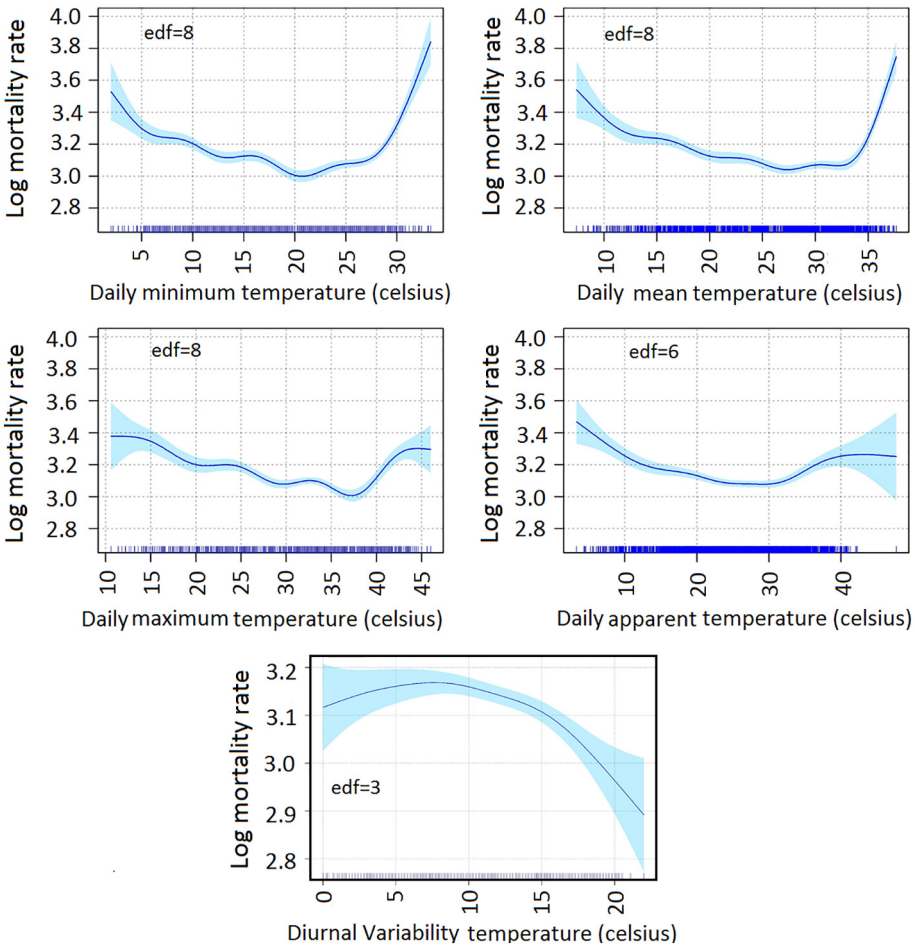

Fig. 8. Exposure-response relationship of maximum, mean, minimum and apparent temperature and diurnal temperature variability.

smoking/alcohol habits, which may serve as effect modifiers. We tried to separate cause specific mortality (RD & CVD), but due to low data count and statistical insignificance, we have avoided reporting case-specific mortality.

4. Conclusions

Present study estimates the health effects of temperature for the city of Varanasi and the additional effect on mortality due to temperature extreme, considering other nonlinear confounding factors e.g. time trends, relative humidity, air quality and days of the week. The major findings support the general fact that high temperature extremes have deleterious impact on human health. In general, daily mean temperature was more strongly associated with mortality than other temperature metrics. This key reference will allow us to formulate a model that provide us the estimates worthy to be considered in mortality risk assessments and reduce the underestimation. The study is first of its kind that present the increase in mortality with decrease in DTV. Our novel application of DTV argue that the attention must be paid to decrease in DTV in setting up early warning system. It was found that the percent increase in mortality was high during summer compared to winter. Similarly, risk ratio was high due to heat wave compared to cold spell. This brings forth the key point for policy making where major emphasis needs to be made in combating the heat related mortality. Interestingly, the negative impact of unusual temperature does not remain restrict to a specific age group instead different temperature metrics influence age differently. Like high mean temperature during summer increased the mortality ≥65 years of age particularly for females, while heat waves and DTV influenced high mortality for 0–4 and cold wave for 5–44 years' age group, females again being more vulnerable. This suggests that females were more vulnerable despite the fact that the total mortality remains much higher for males. The dose response curve explored the nonlinear relation between mortality and different temperature metrics emphasizing increased mortality above certain temperature thresholds. In addition, to test the robustness of the model, sensitivity analysis was performed for temperature-mortality associations accounting nonlinear and delayed (lag) effects of temperature. A change in lag did influence the effect estimates during winter compared to summer. We therefore, conclude with a level of confidence that potential change in climate will have drastic impact on human health in the city of Varanasi, which necessitates proper attention both in prioritizing governmental policies and public awareness.

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Competing interests

The authors declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2019.02.074.

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